

### **REMARKS**

Applicants wish to thank the Examiner for her time during a telephonic interview on February 10, 2003. Reconsideration of the application is respectfully requested in view of the following remarks. Claims 1-54 and 61-67 are pending in the application. No claims have been allowed. Claims 1, 29, 31, 33, 36, 47, 50, 54, 61, and 64 are independent.

### ***Cited Art***

The Action relies on Chen et al. "Ratio-Based Decisions and the Quantitative Analysis of cDNA Microarray Images," Journal of Biomedical Optics, 1997, vol. 2:364-373 ("Chen I"); Jain et al., IEEE Transactions on Pattern Analysis and Machine Intelligence, 2000, vol. 22:4-37 ("Jain"); and Chen et al., Proc. SPIE, 1999, vol. 3602:422-428 ("Chen II").

### ***Patentability of Claims 1-54 and 61-65 under § 112, ¶ 1***

The Action rejects claims 1-54 and 61-65 as containing subject matter not described in such a way as to reasonably convey to one of skill in the art that the inventors had possession of the claimed invention. Applicants present further citations to the Application to illustrate where in the Application the recited language is supported, which indicates that the subject matter is indeed described in a way to reasonably convey that the inventors has possession of the claimed invention at the time the Application was filed.

### ***Claim 1***

For claim 1, the Action points to the language "effectiveness being a quantification of gene relatedness" and "permutations of the plurality of candidate genes" and calls into question whether the recited language is supported by the specification.

*The specification's description of "effectiveness . . . can then be measured to quantify relatedness for genes" supports the claim's recitation of "the effectiveness being a quantification of gene relatedness."* The Action states the present claims "read on the effectiveness as a quantification of relatedness rather than the effectiveness of the model as a whole and there is no basis for this in the specification." Applicants respectfully disagree. Page 3, lines 7-10 of the Application state:

The nonlinear model predicts gene expression among the set of genes. The effectiveness of the nonlinear model in predicting gene expression can then be measured to quantify relatedness for genes in the set.

The Application as filed thus indicates that effectiveness of the model can be measured to quantify relatedness for genes; the claim recites "measuring effectiveness of the nonlinear model." The technique need not indicate the nature of the relationship between the genes. For example, the Application indicates at page 4, lines 8-9:

If the technique indicates a group of genes are related, researchers can then further investigate the group if appropriate.

Given that the specification expressly supports the claim, the Application sufficiently conveys to one of skill in the art that Applicants were in possession of the claimed invention.

*The "predictive elements" language and Table 2 of the specification support the claim's recitation of "permutations of the plurality of candidate genes."* The Action states that the support pointed to refers to permutations of predictive elements for the predicted gene and not a plurality of genes. There is no indication of what the permutations refer to in terms of gene expression." However, the recited language finds support at page 13, lines 15-16 of the Application which state:

At 820, if there are more possible permutations of predictive elements for the predicted gene, the method proceeds to 808.

and at page 13, lines 8-10, which gives examples of "predictive elements":

At 808, a set of predictive elements (e.g., gene expression levels, experimental conditions, or both) are designated for the predicted gene.

Finally, Table 2 shows an example in which various permutations of candidate genes (e.g., G<sub>1</sub>, G<sub>2</sub>, G<sub>3</sub>, G<sub>4</sub>, G<sub>5</sub>, and G<sub>6</sub>) are used as predictors. As stated in the claim, the model is constructed based on data comprising a plurality of gene expression level observations for the plurality of candidate genes.

Accordingly, Applicants find sufficient support for the recited language in the Application, which would convey to one of skill in the art that the inventors were in possession of the invention. For at least these reasons, claim 1 and its dependent claims, 2-28 and 62-63, are allowable under § 112, ¶ 1.

*Claim 65*

Claim 65 includes the language "indicates relatedness within a network controlling gene expression." For example, the Application states at page 6, lines 22 et seq., "The mechanism of the relationship need not be a factor in determining relatedness. In the network that controls gene expression, . . . or they may be distributed about the network in such a way that their relationship is based on chains of interaction . . . "

The language thus finds support in the specification. For these reasons, claim 65 is allowable under § 112, ¶ 1.

*Claim 54*

For claim 54, the Action points to the language "quantification as indicating relatedness" and calls into question whether the recited language is supported by the specification.

*The specification as filed supports "quantification as indicating relatedness."* The Action states, "The specification does not provide information on assessing the quantification of the effectiveness of the model as it relates to gene relatedness." However, page 3, lines 7-10 of the Application state:

The nonlinear model predicts gene expression among the set of genes. The effectiveness of the nonlinear model in predicting gene expression can then be measured to quantify relatedness for genes in the set.

Further, FIG. 11 shows various quantified results with the word "relatedness" to show what the quantifications (e.g., bar graphs) indicate. In the example, a higher quantification (e.g., a larger bar) indicates a greater relatedness.

The Action also indicates, "Just because the genes can be labeled with a value indicating high, or low relatedness, does not give a basis for the system to assess effectiveness of the model." Applicants point to page 6, lines 22-23, which state:

The mechanism of the relationship need not be a factor in determining relatedness.

In other words, the technique can operate without regard to which particular mechanism is involved. The technique can simply be used to quantify the relatedness of a set of genes; the set of genes can then be further investigated by researchers.

The language of claim 54 is thus supported by the application as filed.

### *Claim 50*

Applicants acknowledge the rejection of claim 50; the rejection states that, "The example given refers to a ternary perceptron." However, Applicants respectfully point to page 15, line 7, which states:

The number of inputs can vary and a convention other than ternary can be used. Therefore, the application adequately supports the "nonbinary" language, and would convey to one of skill in the art that the inventors had possession of the invention as claimed.

For this reason, claim 50 and its dependent claims, 51-53 and 66-67, are allowable under § 112, first paragraph.

### *The Remaining Claims*

Applicants find no specific rejection under §112 for the remaining claims and believe they are supported by the application as filed.

### ***Patentability of Claims 1-54 and 61-67 over Chen I, Chen II, and Jain under § 103***

The Action rejects claims 1-54 and 61-65 under 35 U.S.C. § 103(a) as unpatentable over Chen I, Chen II, and Jain. Applicants respectfully submit the claims in their present form are allowable over the cited art. To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. (MPEP § 2142.) In the present case, there is nothing within the references themselves that would lead to a modification that would result in the claimed arrangement, and the references fail to teach or suggest all the claim limitations.

### *Claim 1*

Claim 1 is directed to a method for quantifying gene relatedness and recites in part:

for a plurality of selected permutations of the plurality of candidate genes,  
performing (a)-(c):

(a) based on . . . gene expression level observations . . . constructing a  
nonlinear model predicting gene expression . . . ;

...; and  
presenting a plurality of the quantifications of gene relatedness showing  
relative relatedness for a plurality of the permutations of the genes.

For example, FIG. 11 shows relative relatedness for a plurality of permutations of genes.

*The Action attacks claim 1 by assembling references to show that predicting gene expression (e.g., with neural networks) is obvious, but the claims include more than simply predicting gene expression.* Claim 1 stands rejected over a Chen I-Chen II-Jain combination. While some of the references do contain relevant disclosure concerning gene expression techniques, they lack sufficient disclosure to result in the claimed arrangement. Further, none of the references contain any motivation to somehow modify or combine the references to result in the claimed arrangement. For example, the references do not mention showing relative relatedness for a plurality of the permutations of the genes.

Chen I relates to the quantitative analysis of cDNA Microarray images, and technology related to the article was acknowledged in the Application at page 9, lines 6-8 and page 10, lines 19-21. The techniques of Chen I can be used to determine whether gene expression is up-regulated or down-regulated. Chen can thus be used during generation of gene expression observations. However, Chen I fails to go beyond generating the gene expression observations and does not, for example, contain any disclosure that would lead one to construct a nonlinear model predicting gene expression.

Chen II relates to clustering technologies. For example, in a passage cited by the Action, Chen describes at the abstract:

We propose a K-mean based algorithm in which gene expression levels fluctuate in parallel will be clustered together. The resulting cluster suggests some functional relationships between genes, and some known genes belongs to a unique functional classes shall provide indication for unknown genes in the same clusters.

In other words, the techniques of Chen II can be used to cluster together genes based on an analysis. A description of clustering would not lead one to predicting gene expression. The Action further relies on Chen II's description of a fingerprint gene expression at pages 422-23:

One study carried out in [5] reported that gene expression patterns derived from 7 alveolar Rhabdomyosarcoma cell-lines were clustered together relatively to expression patterns derived from 6 other cancerous cell-lines. This result not only indicates that the gene expression pattern may be used to identify the state of a biological sample, but also demonstrate that a gene expression pattern,

containing tens of thousands of genes, may be represented by a small set of genes, or a *fingerprint* gene expression. Clearly, gene expression patterns along with certain pattern recognition method will lead biologists to understand the biological sample composition, while a set of fingerprint genes will provide a focus-point for further study.

Applicants fail to understand how the above passage would lead one to predicting gene expression and thus conclude that Chen II would not lead one to such an arrangement.

Jain includes discussion of statistical pattern recognition and includes a description of classifiers. For example, Jain describes at page 8:

In the classification mode, the trained classifier assigns the input pattern to one of the pattern classes under consideration based on the measured features.

In other words, the techniques of Jain can be used to assign an input pattern to a class based on measured features. However, Jain also fails to describe constructing a nonlinear model predicting gene expression.

Further, even if Chen I, Chen II, and Jain could somehow be amalgamated into a combined arrangement to predict gene expression, the claim does not recite predicting gene expression *per se*. Rather, the claimed combination is a novel, non-obvious combination that comprises predicting gene expression but also recites showing relative relatedness for a plurality of the permutations of the genes.

The combined references simply would not lead one to present a plurality of the quantifications of gene relatedness showing relative relatedness for a plurality of the permutations of the genes as recited. Applicants fail to find in any of the references a teaching or suggesting to present a plurality of gene relatedness quantifications showing related relatedness for genes.

Accordingly, as understood by Applicants, a *prima facie* case of obviousness cannot be assembled from the three references, and the claims are allowable over them. If the Examiner disagrees, Applicants encourage the Examiner to contact the undersigned attorney to discuss the matter further by telephone.

*Remaining Claims*

The remaining claims contain additional, patentably-distinct subject matter not taught or suggested by the three references. Accordingly, the remaining claims are also allowable at this time.

*Request for Interview*

If any issues remain, the Examiner is formally requested to contact the undersigned attorney prior to issuance of the next Office Action in order to arrange a telephonic interview. It is believed that a brief discussion of the merits of the present application may expedite prosecution. Applicants submit the foregoing formal Amendment so that the Examiner may fully evaluate Applicants' position, thereby enabling the interview to be more focused.

This request is being submitted under MPEP § 713.01, which indicates that an interview may be arranged in advance by a written request.

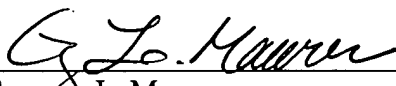
*Conclusion*

The claims in their present form should now be allowable. Such action is respectfully requested.

Respectfully submitted,

KLARQUIST SPARKMAN, LLP

By

  
\_\_\_\_\_  
Gregory L. Maurer  
Registration No. 43,781

One World Trade Center, Suite 1600  
121 S.W. Salmon Street  
Portland, Oregon 97204  
Telephone: (503) 226-7391  
Facsimile: (503) 228-9446

**Marked-up Version of Amended Claims  
Pursuant to 37 C.F.R. §§ 1.121(b)-(c)**

The following claims 66-67 have been added:

66. (New) The method of claim 50 further comprising:  
means for presenting the effectiveness as indicating relatedness for the plurality of  
candidate genes.
67. (New) The method of claim 50 wherein the nonlinear model comprises a ternary  
model.